



## General

### Guideline Title

Early (uncomplicated) Parkinson's disease.

### Bibliographic Source(s)

Oertel WH, Berardelli A, Bloem BR, Bonuccelli U, Burn D, Deuschl G, Dietrichs E, Fabbrini G, Ferreira JJ, Friedman A, Kanovsky P, Kostic V, Nieuwboer A, Odin P, Poewe W, Rascol O, Sampaio C, Schupbach M, Tolosa E, Trenkwalder C. Early (uncomplicated) Parkinson's disease. In: Gilhus NE, Barnes MP, Brainin M, editor(s). European handbook of neurological management. 2nd ed. Vol. 1. Oxford (UK): Wiley-Blackwell; 2011. p. 217-36. [198 references]

### Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Horstink M, Tolosa E, Bonuccelli U, Deuschl G, Friedman A, Kanovsky P, Larsen JP, Lees A, Oertel W, Poewe W, Rascol O, Sampaio C, European Federation of Neurological Societies, Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies and the Movement Disorder Society-European Section. Part I: early (uncomplicated) Parkinson's disease. Eur J Neurol 2006 Nov;13(11):1170-85.

## Regulatory Alert

### FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

#### Drug Withdrawal

- [March 29, 2007 - WITHDRAWAL: Permax \(pergolide\)](#) : Voluntary market withdrawal in the U.S. and worldwide due to safety concerns of an increased risk of cardiovascular events. See the U.S. Food and Drug Administration (FDA) Web site for more information.

## Recommendations

### Major Recommendations

The levels of evidence (Class I-IV) supporting the recommendations and ratings of recommendations (A-C, Good Practice Point [GPP]) are defined at the end of the "Major Recommendations" field.

#### Early Untreated Patients

The optimal time frame for onset of therapy has not been clearly defined. Once parkinsonian signs start to have an impact on the patient's life, initiation of treatment is recommended. For each patient, the choice between the numerous effective drugs available is based on a subtle combination of subjective and objective factors. These factors include considerations related to the drug (efficacy for symptomatic control of parkinsonism/prevention of motor complications, safety, practicality, costs, etc.), to the patient (symptoms, age, needs, expectations, experience, co-morbidity, socioeconomic level, etc.), and to their environment (drug availability according to national markets in the European Union, variability in economic and health insurance systems, etc.). However, based on the available level of evidence alone, two main issues are usually considered when initiating a symptomatic therapy for early Parkinson's disease (PD): the symptomatic control of parkinsonism, and the prevention of motor complications (see table below).

Currently, there is no uniform proposal across Europe on initiating symptomatic medication for PD. Options include starting treatment with:

- *Monoamine oxidase isoenzyme type B (MAO-B inhibitor)*, like selegiline or rasagiline (Level A). The symptomatic effect is more modest than that of levodopa and (probably) dopamine agonists, but they are easy to administer (one dose, once daily, no titration), and well tolerated (especially rasagiline).
- *Amantadine or an anticholinergic* (Level B). The impact on symptoms is smaller than that of levodopa. Anticholinergics are poorly tolerated in the elderly and their use is mainly restricted to young patients.
- *Levodopa*, the most effective symptomatic antiparkinsonian drug (Level A). After a few years of treatment, levodopa is frequently associated with the development of motor complications. As older patients are more sensitive to neuropsychiatric adverse reactions and are less prone to developing motor complications, the early use of levodopa is recommended in the older population (GPP). The early use of controlled release levodopa formulations is not effective in the prevention of motor complications (Level A).
- *Orally active dopamine agonist*. Pramipexole, piribedil, and ropinirole immediate- or controlled-release are effective as monotherapy in early PD (Level A), with a lower risk of motor complications than levodopa for pramipexole or ropinirole (Level A). Older drugs like bromocriptine are supported by lower class evidence, giving a Level B recommendation. However, there is no convincing evidence that they are less effective in managing patients with early PD. The benefit of agonists in preventing motor complications (Level A, with data up to 5 years only) must be balanced with the smaller effect on symptoms and the greater incidence of hallucinations, impulse-control disorders, somnolence, and leg edema, as compared with levodopa. Patients must be informed of these risks (e.g., excessive daytime somnolence is especially relevant to drivers). Younger patients are more prone to developing levodopa-induced motor complications, and therefore initial treatment with an agonist can be recommended in this population (GPP). Ergot derivatives such as pergolide, bromocriptine, and cabergoline are not recommended as first-line medication because of the risk of fibrotic reactions. Rotigotine is administered transdermally using a patch and ropinirole controlled-release (CR) once daily orally, as opposed to the other agonists that are administered orally three times a day. Subcutaneous apomorphine is not appropriate at this stage of the disease. The early combination of low doses of a dopamine agonist with low doses of levodopa is another option, although the benefits of such a combination have not been properly documented.
- *Rehabilitation*. Due to the lack of evidence of the efficacy of physical therapy and speech therapy at the early stage of the disease, a recommendation cannot be made.

Table. Recommendations for the Treatment of Early PD

Therapeutic Interventions	Recommendation Level	
	Symptomatic Control of Parkinsonism	Prevention of Motor Complications
Levodopa	Effective (Level A)	Not applicable
Levodopa controlled release (CR)	Effective (Level A)	Ineffective (Level A)
Apomorphine	Not used <sup>a</sup>	Not used <sup>a</sup>
Bromocriptine <sup>b</sup>	Effective (Level B)	Effective (Level B)
Cabergoline <sup>b</sup>	Effective (Level B)	Effective (Level A)
Dihydroergocryptine <sup>b</sup>	Effective (Level A)	No recommendation <sup>c</sup>
Lisuride <sup>b</sup>	Effective (Level B)	Effective (Level C)

Pergolide <sup>b*</sup>	Recommendation Level Effective (Level A)	Effective (Level B)
Therapeutic Interventions	Symptomatic Control of Parkinsonism	Prevention of Motor Complications
Piribedil	Effective (Level C)	No recommendation <sup>c</sup>
Pramipexole	Effective (Level A)	Effective (Level A)
Pramipexole CR <sup>e</sup>	Not available	Not available
Ropinirole	Effective (Level A)	Effective (Level A)
Ropinirole CR <sup>e</sup>	Effective (Level A)	No recommendation <sup>c</sup>
Rotigotine <sup>f</sup>	Effective (Level A)	No recommendation <sup>c</sup>
Selegiline	Effective (Level A)	Ineffective (Level A)
Rasagiline	Effective (Level A)	No recommendation <sup>c</sup>
Entacapone <sup>d</sup>	No recommendation <sup>c</sup>	No recommendation <sup>c</sup>
Tolcapone <sup>d</sup>	No recommendation <sup>c</sup>	No recommendation <sup>c</sup>
Amantadine	Effective (Level B)	No recommendation <sup>c</sup>
Anticholinergics	Effective (Level B)	No recommendation <sup>c</sup>
Rehabilitation	No recommendation <sup>c</sup>	No recommendation <sup>c</sup>
Surgery	Not used	Not used

<sup>a</sup>Subcutaneous apomorphine is not used in early PD.

<sup>b</sup>Pergolide\*, bromocriptine, cabergoline and, precautionarily, other ergot derivatives, cannot be recommended as a first-line treatment for early PD because of the risk of valvular heart disorder (Rascol et al., "New concerns," 2004; Rascol et al., "Dopamine agonists," 2004).

<sup>c</sup>No recommendation can be made due to insufficient data .

<sup>d</sup>As catechol-O-methyltransferase (COMT) inhibitors, entacapone and tolcapone should always be given with levodopa. Due to hepatic toxicity, tolcapone is not recommended in early PD.

<sup>e</sup>Controlled-release.

<sup>f</sup>Transdermal patch delivery system

\*Note from the National Guideline Clearinghouse (NGC): On March 29, 2007, Permax (pergolide) was withdrawn from the market in the U.S. and worldwide due to safety concerns of an increased risk of cardiovascular events. See the [U.S. Food and Drug Administration \(FDA\) Web site](#)  for more information.

#### Adjustment of Initial Monotherapy in Patients without Motor Complications

##### *Patients Not on Dopaminergic Therapy*

If a patient has started on a monoamine oxidase isoenzyme B (MAO-B) inhibitor, anticholinergic, amantadine, or a combination of these drugs, a stage will come when, because of worsening motor symptoms, there is a requirement for:

- Addition of levodopa or a dopamine agonist (GPP). Just like in *de novo* patients, at this stage, the choice between levodopa and an agonist again mainly depends on the impact of improving motor disability (better with levodopa) compared with the risk of motor complications (less with agonists in the first 3 to 5 years) and neuropsychiatric complications (greater with agonists). In addition, there is the effect of age on the occurrence of motor complications (more frequent in younger patients), and neuropsychiatric/behavioural complications (more frequent in older and cognitively impaired patients). In general, dopaminergic therapy may/could be started with agonists in younger patients,

whereas levodopa may be preferred in older patients (GPP, see previous section) and in multimorbid patients of any age.

### *Patients on Dopaminergic Therapy*

Once receiving therapy with a dopamine agonist or levodopa, adjustments of these drugs will also become necessary over time because of worsening motor symptoms.

If on dopamine agonist therapy:

- Increase the dopamine agonist dose (GPP). However, even when the dopamine agonist dose is increased over time, it cannot control parkinsonian symptoms for more than about 3 to 5 years of follow-up in most patients.
- Switch between dopamine agonists (Level C).
- Add levodopa (GPP).

If on levodopa:

- Increase the levodopa dose (GPP).
- Add a dopamine agonist (GPP), although the efficacy of adding an agonist has been insufficiently evaluated.
- Add a COMT-inhibitor to levodopa at the transition of a non-fluctuating to a fluctuating status, i.e., if motor fluctuations evolve (GPP) – preferably in older patients and multimorbid patients of any age.

### *Patients with Persistent or Emerging Disabling Tremor*

If a significant tremor persists despite usual therapy with dopaminergic agents or amantadine, the following treatment options exist for tremor at rest:

- Anticholinergics (GPP: possibly useful, although no full consensus could be made). Cave: anticholinergic side effects, particularly cognitive dysfunction in older patients. (See the "Potential Harms" field.)
- Clozapine (Level B) (Bonuccelli et al., 1997; Friedman et al., 1997; "Low-dose clozapine," 1999). Due to safety concerns (see the National Guideline Clearinghouse [NGC] summary of the European Federation of Neurological Societies [EFNS] guideline [Late \[Complicated\] Parkinson's Disease](#) on psychosis), clozapine is not advised for routine use, but it is considered as an experimental approach for exceptionally disabled patients requiring specialized monitoring (GPP).
- Beta-blockers (propranolol). Beta-blockers can be effective in both resting and postural tremor (Level C) (Marsden, Parkes, & Rees, 1974; Foster et al., 1984; Koller & Herbst, 1987; Henderson et al., 1994). However, due to methodological problems, a Cochrane review found it impossible to determine whether beta-blocker therapy is effective for tremor in PD (Crosby, Deane, & Clarke, 2003). Further studies are needed to judge the efficacy of beta-blockers in the treatment of tremor in PD (no recommendation can be made).
- Consider deep brain stimulation. Usually subthalamic nucleus stimulation, rarely thalamic stimulation (GPP; see the NGC summary of the EFNS guideline [Late \[Complicated\] Parkinson's Disease](#) on psychosis).

### Definitions:

#### Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

- a. Randomization concealment
- b. Primary outcome(s) is/are clearly defined
- c. Exclusion/inclusion criteria are clearly defined
- d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
- e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

#### Rating of Recommendations

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good Practice Point If the evidence is based on expert opinion and scientific evidence is lacking and therefore the rating of recommendation is below C, best practice is recommended (Good Practice Point).

## Clinical Algorithm(s)

None provided

## Scope

### Disease/Condition(s)

Early (uncomplicated) Parkinson's disease (PD)

### Guideline Category

Assessment of Therapeutic Effectiveness

Prevention

Treatment

### Clinical Specialty

Family Practice

Geriatrics

Internal Medicine

Neurology

Pharmacology

### Intended Users

Physicians

### Guideline Objective(s)

To provide scientifically supported recommendations for the management of early (uncomplicated) Parkinson's disease (PD)

### Target Population

Patients with early (uncomplicated) Parkinson's disease

## Interventions and Practices Considered

1. Monoamine oxidase isoenzyme B (MAO-B) inhibitors (e.g., selegiline, rasagiline)
2. Amantadine
3. Anticholinergics
4. Levodopa
5. Orally active dopamine agonists (e.g., pramipexole, ropinirole, bromocriptine)
6. Adjustment of initial monotherapy

Note: Refer to the original guideline document for information on medications and practices that were considered but not recommended due to ineffectiveness, insufficient data, or serious adverse effects.

## Major Outcomes Considered

Effectiveness of treatment in symptomatic control of parkinsonism and prevention of motor and non-motor complications  
Adverse effects of medications

## Methodology

### Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

### Description of Methods Used to Collect/Select the Evidence

Searches were made in Medline, the full database of the Cochrane Library, and the International Network of Agencies for Health Technology Assessment (INAHTA). The databases were also searched for existing guidelines and management reports, and requests were made to European Federation of Neurological Societies (EFNS) for their National Guidelines. For the 2010 update, the Movement Disorder Society's Evidence Based Medicine Task Force conducted systematic checking of reference lists published in review articles and other clinical reports, and provided the results of a literature search for articles published until September 2009.

### Number of Source Documents

Not stated

### Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

### Rating Scheme for the Strength of the Evidence

Evidence Classification Scheme for a Therapeutic Intervention

Class I: An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required:

- a. Randomization concealment
- b. Primary outcome(s) is/are clearly defined
- c. Exclusion/inclusion criteria are clearly defined
- d. Adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias
- e. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences

Class II: Prospective matched-group cohort study in a representative population with masked outcome assessment that meets a–e above or a randomized, controlled trial in a representative population that lacks one criteria a–e

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

## Description of the Methods Used to Analyze the Evidence

Classification of scientific evidence is made according to the European Federation of Neurological Societies (EFNS) guidance (see the "Availability of Companion Documents" field).

## Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

Classification of scientific evidence and the rating of recommendations are made according to the European Federation of Neurological Societies (EFNS) guidance (see the "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for the Strength of the Recommendations" fields). The original guideline focuses on the highest levels of evidence available. If the level of available evidence is only Level IV, i.e., if the evidence is based on the experience of the guidelines development group (expert opinion) and/or scientific evidence is lacking and therefore the rating of recommendation is below C, best practice is recommended (Good Practice Point [GPP]).

Meetings of the original author group were held in Chicago in June 2008 and in Paris in May 2009 to agree the strategy for revision of the original review, and additional members were invited to join the author group. Two authors were assigned to review the recent publications relating to each section of the original document, grade the evidence, and make any necessary revisions.

## Rating Scheme for the Strength of the Recommendations

Rating of Recommendations

Level A rating (established as effective, ineffective, or harmful) requires at least one convincing class I study or at least two consistent, convincing class II studies.

Level B rating (probably effective, ineffective, or harmful) requires at least one convincing class II study or overwhelming class III evidence.

Level C rating (possibly effective, ineffective, or harmful) requires at least two convincing class III studies.

Good Practice Point If the evidence is based on expert opinion and scientific evidence is lacking and therefore the rating of recommendation is below C, best practice is recommended (Good Practice Point).

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

Peer Review

## Description of Method of Guideline Validation

The guidelines were validated according to the European Federation of Neurological Societies (EFNS) criteria (see the "Availability of Companion Documents" field).

## Evidence Supporting the Recommendations

### References Supporting the Recommendations

Bonuccelli U, Ceravolo R, Salvetti S, D'Avino C, Del Dotto P, Rossi G, Murri L. Clozapine in Parkinson's disease tremor. Effects of acute and chronic administration. *Neurology*. 1997 Dec;49(6):1587-90. [PubMed](#)

Crosby NJ, Deane KH, Clarke CE. Beta-blocker therapy for tremor in Parkinson's disease. *Cochrane Database Syst Rev*. 2003; (1):CD003361. [28 references] [PubMed](#)

Foster NL, Newman RP, LeWitt PA, Gillespie MM, Larsen TA, Chase TN. Peripheral beta-adrenergic blockade treatment of parkinsonian tremor. *Ann Neurol*. 1984 Oct;16(4):505-8. [PubMed](#)

Friedman JH, Koller WC, Lannon MC, Busenbark K, Swanson-Hyland E, Smith D. Benztropine versus clozapine for the treatment of tremor in Parkinson's disease. *Neurology*. 1997 Apr;48(4):1077-81. [PubMed](#)

Henderson JM, Yiannikas C, Morris JG, Einstein R, Jackson D, Byth K. Postural tremor of Parkinson's disease. *Clin Neuropharmacol*. 1994 Jun;17(3):277-85. [PubMed](#)

Koller WC, Herberger G. Adjuvant therapy of parkinsonian tremor. *Arch Neurol*. 1987 Sep;44(9):921-3. [PubMed](#)

Low-dose clozapine for the treatment of drug-induced psychosis in Parkinson's disease. The Parkinson Study Group. *N Engl J Med*. 1999 Mar 11;340(10):757-63. [PubMed](#)

Marsden CD, Parkes JD, Rees JE. Letter: Propranolol in Parkinson's disease. *Lancet*. 1974 Aug 17;2(7877):410. [PubMed](#)

Rascol O, Pathak A, Bagheri H, Montastruc JL. Dopaminergics and fibrotic valvular heart disease: further considerations. *Mov Disord*. 2004 Dec;19(12):1524-5. [PubMed](#)



## Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

Appropriate treatment of early Parkinson's disease

### Potential Harms

- The most commonly reported side effects of *anticholinergics* are blurred vision, urinary retention, nausea, constipation (rarely leading to paralytic ileus), and dry mouth. The incidence of reduced sweating, particularly in those patients on neuroleptics, can lead to fatal heat stroke. Impaired mental function (mainly immediate memory and memory acquisition) and acute confusional state are a well-documented central side effect that resolves after drug withdrawal. The abrupt withdrawal of anticholinergics may lead to a rebound effect with marked deterioration of parkinsonism. Consequently, anticholinergics should be discontinued gradually and with caution.
- As with any dopaminergic drug, *monoamine oxidase isoenzyme type B (MAO-B) inhibitors* can induce a variety of dopaminergic adverse reactions. At the daily doses of selegiline currently recommended, the risk of tyramine-induced hypertension (the 'cheese effect') is low. Concerns that the selegiline/levodopa combination increased mortality rates have been allayed.
- Side effects of *amantadine* are generally mild, most frequently including dizziness, anxiety, impaired coordination and insomnia (>5%), nausea and vomiting (5% to 10%), peripheral distal oedema (unresponsive to diuretics), and headache, nightmares, ataxia, confusion/agitation, drowsiness, constipation/diarrhoea, anorexia, xerostomia, and livedo reticularis (<5%). Less common side effects include psychosis, abnormal thinking, amnesia, slurred speech, hyperkinesia, epileptic seizures (rarely, and at higher doses), hypertension, urinary retention, decreased libido, dyspnoea, rash, and orthostatic hypotension (during chronic administration).
- Catechol-O-methyltransferase (COMT) inhibitors increase levodopa bioavailability, so they can increase the incidence of dopaminergic adverse reactions, including nausea, and cardiovascular and neuropsychiatric complications. Diarrhoea and urine discolouration are the most frequently reported non-dopaminergic adverse reactions.
- Peripheral side effects of *levodopa* include gastrointestinal and cardiovascular dysfunction. Central adverse effects include levodopa motor problems such as fluctuations, dyskinesia and dystonia, and psychiatric side effects such as confusion, hallucinations and sleep disorders. A meta-analysis found approximately 40% likelihood of motor fluctuations and dyskinesias after 4 to 6 years of levodopa therapy. Risk factors are younger age, longer disease duration, and levodopa. In individual studies, the percentage of fluctuations and dyskinesia may range from 10% to 60% of patients at 5 years, and up to 80% to 90% in later years. Neuropsychiatric complications occur in less than 5% of *de novo* patients on levodopa monotherapy.
- Side effects such as nausea, vomiting, orthostatic hypotension, confusion, psychosis, and somnolence may occur with administration of any of *dopamine agonists and other active dopamine-mimetic medications*. Peripheral leg oedema is also commonly observed with most agonists. Hallucinations and somnolence are more frequent with some agonists than with levodopa, even in healthy subjects, in the case of somnolence. Though there is no convincing evidence that any agonist is better tolerated than bromocriptine, a recent meta-analysis suggested that while frequencies of somnolence, hallucination, or anxiety cases were higher with non-ergot dopamine agonists (DAs), incidence of vomiting, arterial hypotension, or depression was higher with ergots. The rare but severe risk of pleuropulmonary/retroperitoneal fibrosis is greater with ergot agonists than with non-ergot agonists. The same is true for valvular heart disorders. As pergolide and cabergoline have been the most frequently reported drugs at the present time, they are only used as a second-line alternative option, when other agonists have not provided an adequate response. If employed, regular monitoring of heart valves by ultrasound is mandatory. Impulse-control disorders have recently been identified as a common adverse drug reaction to dopamine agonists. Prevalence ranges between 5% and 15% depending on the author. The principal risk factor is treatment with dopamine agonists, although they can occur on levodopa as well. Personal traits, disturbed decision-making abilities, and younger age have also been implicated. Comorbidities, cognitive impairment, disease severity, and polytherapy are sometimes also mentioned. Up to the present there is no evidence about between-agonists difference in the frequency of these events.

# Contraindications

## Contraindications

- *Anticholinergics* are contraindicated in patients with narrow-angle glaucoma, tachycardia, dementia, hypertrophy of the prostate, gastrointestinal obstruction, and megacolon.
- For recommendations concerning drug dosage, method and route of administration, and contraindications, the reader is referred to the local formulary or the manufacturer's instruction except when provided within the guideline recommendations.

# Qualifying Statements

## Qualifying Statements

- This guideline provides the view of an expert task force appointed by the Scientific Committee of the European Federation of Neurological Societies (EFNS). It represents a peer-reviewed statement of minimum desirable standards for the guidance of practice based on the best available evidence. It is not intended to have legally binding implications in individual cases.
- For recommendations concerning drug dosage, method and route of administration, and contraindications the reader is referred to the local formulary or manufacturer's instruction, except when provided within the guidelines' recommendation itself.

# Implementation of the Guideline

## Description of Implementation Strategy

The European Federation of Neurological Societies has a mailing list and all guideline papers go to national societies, national ministries of health, World Health Organisation, European Union, and a number of other destinations. Corporate support is recruited to buy large numbers of reprints of the guideline papers and permission is given to sponsoring companies to distribute the guideline papers from their commercial channels, provided there is no advertising attached.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

## IOM Care Need

Living with Illness

## IOM Domain

Effectiveness

# Identifying Information and Availability

## Bibliographic Source(s)

V, Nieuwboer A, Odin P, Poewe W, Rascol O, Sampaio C, Schupbach M, Tolosa E, Trenkwalder C. Early (uncomplicated) Parkinson's disease. In: Gilhus NE, Barnes MP, Brainin M, editor(s). European handbook of neurological management. 2nd ed. Vol. 1. Oxford (UK): Wiley-Blackwell; 2011. p. 217-36. [198 references]

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2006 Nov (revised 2011)

## Guideline Developer(s)

European Academy of Neurology - Medical Specialty Society

## Source(s) of Funding

European Federation of Neurological Societies

Financial support from MDS - ES, EFNS and Stichting De Regenboog (the Netherlands – review 2006) and Competence Network Parkinson (Germany – review 2010).

## Guideline Committee

European Federation of Neurological Societies Task Force on Early (Uncomplicated) Parkinson's Disease

## Composition of Group That Authored the Guideline

*Task Force Members:* W. H. Oertel, Philipps-University of Marburg, Centre of Nervous Diseases, Germany; A. Berardelli, Sapienza, Università di Roma, Italy; B. R. Bloem, Donders Institute for Brain, Cognition and Behavior, Radboud University Nijmegen Medical Center, The Netherlands; U. Bonuccelli, University of Pisa, Italy; D. Burn, Institute for Ageing and Health, Newcastle University, Newcastle upon Tyne, UK; G. Deuschl, Christian-Albrechts-University Kiel, Germany; E. Dietrichs, Oslo University Hospital and University of Oslo, Norway; G. Fabbri, Sapienza, Università di Roma, Italy; J. J. Ferreira, Institute of Molecular Medicine, Lisbon, Portugal; A. Friedman, Medical University of Warsaw, Poland; P. Kanovsky, Palacky University, Olomouc, Czech Republic; V. Kostic, Institute of Neurology CCS, School of Medicine, University of Belgrade, Serbia; A. Nieuwboer, Katholieke Universiteit Leuven, Leuven, Belgium; P. Odin, Central Hospital Bremerhaven, Germany, and University Hospital, Lund, Sweden; W. Poewe, Innsbruck Medical University, Austria; O. Rascol, University Hospital and University of Toulouse, Toulouse, France; C. Sampaio, Laboratório de Farmacologia Clínica e Terapêutica e Instituto de Medicina Molecular, Faculdade de Medicina de Lisboa, Portugal; M. Schupbach, INSERM CIC- 9503, Hôpital Pitié-Salpêtrière, Paris, France, and Bern University Hospital and University of Bern, Switzerland; E. Tolosa, Universitat de Barcelona, Spain; C. Trenkwalder, Paracelsus - Elena Hospital, Kassel, and University of Goettingen, Germany

## Financial Disclosures/Conflicts of Interest

A. Berardelli has received speaker honoraria from Allergan and Boehringer Ingelheim.

U. Bonuccelli has acted as scientific advisor for, or obtained speaker honoraria from, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Pfizer, and Schwarz-Pharma. He has received departmental grants and performed clinical studies for Boehringer Ingelheim, Chiesi, Eisai, GlaxoSmithKline, Novartis, Schwarz-Pharma, and Teva.

D. Burn has served on medical advisory boards for Teva, Boehringer-Ingelheim, Archimedes, and Merck Serono. He has received honoraria to

speak at meetings from Teva-Lundbeck, Orion, Boehringer- Ingelheim, GlaxoSmithKline, Novartis, Eisai, UCB, and GE Healthcare.

G. Deuschl has acted as scientific advisor for, or obtained speaker honoraria from, Orion, Novartis, Boehringer Ingelheim, and Medtronic.

E. Dietrichs has received honoraria for lecturing and/or travelling grants from GlaxoSmithKline, Lundbeck, Medtronic, Orion, Solvay, and UCB.

G. Fabbri has received honoraria for lectures from Boehringer Ingelheim, Glaxo Pharmaceuticals, and Novartis Pharmaceuticals, and is member of an advisory board for Boehringer Ingelheim.

J. Ferreira has received honoraria for lecturing and/or consultancy from GlaxoSmithKline, Novartis, Teva, Lundbeck, Solvay, and BIAL.

Andrzej Friedman received honoraria for presentations at educational conferences from Roche Poland, MSD Poland, and Allergan Poland.

P. Kanovsky has received honoraria for lectures from Ipsen and GSK, and received a research grant from Novartis.

V. Kostic has received honoraria for lecturing from Novartis, Boehringer Ingelheim, Merck, Lundbeck, and GlaxoSmithKline, and is a member of the Regional South-Eastern European Pramipexole Advisory Board of Boehringer Ingelheim.

P. Odin has received honoraria for lectures from Boehringer Ingelheim, UCB, GSK, Solvay, and Cephalon, and participated in advisory boards for Boehringer Ingelheim, Cephalon, and Solvay.

W.H. Oertel has received honoraria for consultancy and presentations from Bayer-Schering, Boehringer Ingelheim, Cefalon, Desitin, GlaxoSmithKline, Medtronic, Merck-Serono, Neurosearch, Novartis, Orion Pharma, Schwarz-Pharma Neuroscience, Servier, Synosia, Teva, UCB, and Vifor Pharma.

W. Poewe has received honoraria for lecturing and advisory board membership from Novartis, GlaxoSmithKline, Teva, Boehringer Ingelheim, Schwarz, and Orion.

O. Rascol has received scientific grants and consulting fees from GlaxoSmithKline, Novartis, Boehringer Ingelheim, Eli Lilly, Teva Neuroscience, Eisai, Schering, Solvay, XenoPort, Oxford BioMedica, Movement Disorder Society, UCB, Lundbeck, Schwarz-Pharma, and Servier.

C. Sampaio has received departmental research grants from Novartis Portugal. Her department has also charged consultancy fees to Servier and Lundbeck, and she has received honoraria for lectures from Boehringer Ingelheim.

M. Schüpbach has received speaker's honoraria and travel reimbursement from Medtronic.

E. Tolosa has received honoraria for lectures from Boehringer Ingelheim, Novartis, UCB, GlaxoSmithKline, Solvay, Teva, and Lundbeck, and participated in advisory boards for Boehringer Ingelheim, Novartis, Teva, and Solvay.

C. Trenkwalder has received honoraria for lectures from Boehringer Ingelheim, UCB, Glaxo Pharmaceuticals, and AstraZeneca, and is member of advisory boards for Boehringer Ingelheim, UCB, Cephalon, Solvay, Novartis, and Teva/Lundbeck.

## Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Horstink M, Tolosa E, Bonuccelli U, Deuschl G, Friedman A, Kanovsky P, Larsen JP, Lees A, Oertel W, Poewe W, Rascol O, Sampaio C, European Federation of Neurological Societies, Movement Disorder Society-European Section. Review of the therapeutic management of Parkinson's disease. Report of a joint task force of the European Federation of Neurological Societies and the Movement Disorder Society-European Section. Part I: early (uncomplicated) Parkinson's disease. Eur J Neurol 2006 Nov;13(11):1170-85.

## Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the [European Federation of Neurological Societies \(EFNS\) Web site](#)

## Availability of Companion Documents

The following is available:

- Brainin M, Barnes M, Baron JC, Gilhus NE, Hughes R, Selmaj K, Waldemar G; Guideline Standards Subcommittee of the EFNS Scientific Committee. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces – revised recommendations 2004. Eur J Neurol. 2004 Sep;11(9):577-81. Electronic copies: Available in Portable Document Format (PDF) from the [European Federation of Neurological Societies Web site](#) .

## Patient Resources

None available

## NGC Status

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